

WEST Search History

DATE: Wednesday, February 21, 2007

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>	
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<input type="checkbox"/>	L6	L5 same (progenitor or stem)	0
<input type="checkbox"/>	L5	'Lundgren-Akerlund'-Evy.in.	5
<input type="checkbox"/>	L4	9951639.pn.	3
<input type="checkbox"/>	L3	200075187.pn.	2
<input type="checkbox"/>	L2	0075187.pn.	2
<input type="checkbox"/>	L1	2005253442.pn.	2

END OF SEARCH HISTORY

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(FILE 'HOME' ENTERED AT 07:52:34 ON 21 FEB 2007)

FILE 'DISSABS, 1MOBILITY, AGRICOLA, AQUASCI, BIOTECHNO, COMPENDEX,
COMPUAB, CONFSCI, ELCOM, HEALSAFE, IMSDRUGCONF, INSPEC, LIFESCI, OCEAN,
PAPERCHEM2, PASCAL, POLLUAB, SOLIDSTATE, ADISCTI, ADISINSIGHT, ADISNEWS,
ANABSTR, ANTE, AQUALINE, BIOENG, BIOSIS, ...' ENTERED AT 07:52:59 ON 21
FEB 2007

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L2      200 S L1 (S) (ALPHA (A) (11 OR 10))
L3      138 DUP REM L2 (62 DUPLICATES REMOVED)
L4      85 S MESENCHYM? (S) (ALPHA (A) (11 OR 10 OR MT))
L5      53 DUP REM L4 (32 DUPLICATES REMOVED)
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          SET DETAIL LOGIN
L6      109 S L3 NOT L5
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ANSWER 36 OF 53 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 2000:881196 CAPLUS
 DOCUMENT NUMBER: 134:38626
 TITLE: Cloning, characterization and physiological and
 therapeutic uses of human integrin heterodimer and its
 novel subunit α 11
 INVENTOR(S): Gullberg, Donald
 PATENT ASSIGNEE(S): Active Biotech AB, Swed.
 SOURCE: PCT Int. Appl., 78 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075187	A1	20001214	WO 2000-SE1135	20000531
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2375876	A1	20001214	CA 2000-2375876	20000531
EP 1181317	A1	20020227	EP 2000-939232	20000531
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2003501077	T	20030114	JP 2001-502468	20000531
AU 770652	B2	20040226	AU 2000-54355	20000531
JP 2006246894	A	20060921	JP 2006-119501	20060424
PRIORITY APPLN. INFO.:			SE 1999-2056	A 19990603
			JP 2001-502468	A3 20000531
			WO 2000-SE1135	W 20000531

AB A recombinant or isolated integrin heterodimer comprising a novel subunit α 11 in association with a subunit β is described. The full-length cDNA for this integrin subunit, α 11, has been isolated. The open reading frame of the cDNA encodes a precursor of 1188 amino acids. The predicted mature protein of 1166 amino acids contains 7 conserved FG-GAP repeats, an I-domain with a MIDAS motif, a short transmembrane region and a unique cytoplasmic domain of 24 amino acids containing the sequence GFFRS. The presence of 22 inserted amino acids in the extracellular stalk portion (amino acids 804-826) distinguishes the α 11 integrin sequence from other integrin α -chains. Fluorescence in situ hybridization maps the integrin α 11 gene to chromosome 15q23, in the vicinity of an identified locus for Bardet-Biedl syndrome. Based on Northern blotting integrin α 11 mRNA levels are high in adult human uterus and in heart, and intermediate in skeletal muscle and some other tissues tested. During in vitro myogenic differentiation, α 11 mRNA and protein are up-regulated. Studies of ligand binding properties show that α 11 binds collagen type I Sepharose and cultured muscle cells localize α 11 into focal contacts on collagen type I. The integrin or the subunit α 11 can be used as marker or target of all types of cells. The integrin or subunit α 11 thereof can be used as marker or target in different physiol. or therapeutic methods. They can also be used as active ingredients in pharmaceutical compns. and vaccines.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Mesenchyme
 (stem cell; cloning, characterization and physiol. and therapeutic uses of human integrin heterodimer and its novel subunit α

L5 ANSWER 34 OF 53 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2001:32844310 BIOTECHNO

TITLE: .alpha.11 β 1 integrin is a
receptor for interstitial collagens involved in cell
migration and collagen reorganization on
mesenchymal nonmuscle cells

AUTHOR: Tiger C.-F.; Fougereousse F.; Grundstrom G.; Veiling
T.; Gullberg D.

CORPORATE SOURCE: D. Gullberg, Department of Medical Biochemistry,
Biomedical Center, Uppsala University, S-75123
Uppsala, Sweden.

SOURCE: E-mail: donald.gullberg@icm.uu.se
Developmental Biology, (01 SEP 2001), 237/1 (116-129),
73 reference(s)

DOCUMENT TYPE: CODEN: DEBIAO ISSN: 0012-1606
Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AB .alpha.11 β 1 integrin constitutes a recent
addition to the integrin family. Here, we present the first in vivo
analysis of .alpha.11 protein and mRNA distribution
during human embryonic development. .alpha.11 protein
and mRNA were present in various mesenchymal cells around the
cartilage anlage in the developing skeleton in a pattern similar to that
described for the transcription factor scleraxis, .alpha.
11 was also expressed by mesenchymal cells in
intervertebral discs and in keratocytes in cornea, two sites with highly
organized collagen networks. Neither .alpha.11 mRNA
nor .alpha.11 protein could be detected in myogenic
cells in human embryos. The described expression pattern is compatible
with .alpha.11 β 1 functioning as a receptor for
interstitial collagens in vivo. To test this hypothesis in vitro,
full-length human .alpha.11 cDNA was stably
transfected into the mouse satellite cell line C2C12, lacking endogenous
collagen receptors, .alpha.11 β 1 mediated cell
adhesion to collagens I and IV (with a preference for collagen I) and
formed focal contacts on collagens. In addition, .alpha.
11 β 1 mediated contraction of fibrillar collagen gels in a
manner similar to α 2 β 1, and supported migration on collagen I
in response to chemotactic stimuli. Our data support a role for .
alpha.11 β 1 as a receptor for interstitial
collagens on mesenchymally derived cells and suggest a
multifunctional role of .alpha.11 β 1 in the
recognition and organization of interstitial collagen matrices during
development. .COPYRGT. 2001 Academic Press.

TI .alpha.11 β 1 integrin is a receptor for
interstitial collagens involved in cell migration and collagen
reorganization on mesenchymal nonmuscle cells

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addition to the integrin family. Here, we present the first in vivo
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and mRNA were present in various mesenchymal cells around the
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intervertebral discs and in keratocytes in cornea, two sites with highly
organized collagen networks. Neither .alpha.11 mRNA
nor .alpha.11 protein could be detected in myogenic
cells in human embryos. The described expression pattern is compatible
with .alpha.11 β 1 functioning as a receptor for

interstitial collagens in vivo. To test this hypothesis in vitro, full-length human $\alpha 11$ cDNA was stably transfected into the mouse satellite cell line C2C12, lacking endogenous collagen receptors, $\alpha 11\beta 1$ mediated cell adhesion to collagens I and IV (with a preference for collagen I) and formed focal contacts on collagens. In addition, $\alpha 11\beta 1$ mediated contraction of fibrillar collagen gels in a manner similar to $\alpha 2\beta 1$, and supported migration on collagen I in response to chemotactic stimuli. Our data support a role for $\alpha 11\beta 1$ as a receptor for interstitial collagens on mesenchymally derived cells and suggest a multifunctional role of $\alpha 11\beta 1$ in the recognition and organization of interstitial collagen matrices during development. .COPYRG. 2001 Academic Press.

L5 ANSWER 32 OF 53 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2002:35248276 BIOTECHNO
TITLE: Analysis of the human integrin $\alpha 11$ gene (ITGA11)
and its promoter
AUTHOR: Zhang W.-M.; Popova S.N.; Bergman C.; Velling T.;
Gullberg M.K.; Gullberg D.
CORPORATE SOURCE: D. Gullberg, Department of Medical Biochemistry,
Biomedical Center, Uppsala University, Husargatan 3,
S-751 23 Uppsala, Sweden.
E-mail: donald.gullberg@imbim.uu.se
SOURCE: Matrix Biology, (2002), 21/6 (513-523), 46
reference(s)
CODEN: MTBOEC ISSN: 0945-053X
PUBLISHER ITEM IDENT.: S0945053X02000549
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Integrin .alpha.11 β 1 is a collagen receptor
which is expressed in a subset of mesenchymally-derived tissues
during embryogenesis. Based on available human chromosome 15-derived
sequences and genomic PCR, the complete exon structure of ITGA11,
including the proximal promoter, was assembled into 30 exons. The
inserted region (encoding amino acids 804-826) distinguishing .
alpha.11 from other integrin α chains, was placed
in the very beginning of exon 20. PCR data failed to show alternative
splicing of RNA transcribed from this region. Using the oligo-capping
technique a major transcription start site was mapped 30 nucleotides
upstream of the translation start and identified as an abbreviated
initiator sequence. Promoter sequence analysis in silico suggested the
presence of multiple binding sites for transcription factors in the
region upstream of the transcription start. 3 kb of the 5' flanking
sequence was isolated and used to generate luciferase promoter
constructs. In the fibrosarcoma cell line HT1080 a core promoter [nt
(-)127-(+)25], a potential silencer region [nt (-)400-(-)127] and a
potential enhancer region [nt (-)1519-(-)400], were identified as being
important for .alpha.11 transcription in
mesenchymal cells. Furthermore, studies of the promoter region
will provide valuable information regarding the molecular mechanisms
underlying the cell- and tissue- specific expression pattern of ITGA11.
.COPYRGT. 2002 Elsevier Science B.V. and International Society of Matrix
Biology. All rights reserved.
AB Integrin .alpha.11 β 1 is a collagen receptor
which is expressed in a subset of mesenchymally-derived tissues
during embryogenesis. Based on available human chromosome 15-derived
sequences and genomic PCR, the complete exon structure of ITGA11,
including the proximal promoter, was assembled into 30 exons. The
inserted region (encoding amino acids 804-826) distinguishing .
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in the very beginning of exon 20. PCR data failed to show alternative.
. (-)127-(+)25], a potential silencer region [nt (-)400-(-)127] and a
potential enhancer region [nt (-)1519-(-)400], were identified as being
important for .alpha.11 transcription in
mesenchymal cells. Furthermore, studies of the promoter region
will provide valuable information regarding the molecular mechanisms
underlying the cell- and tissue- . . .

L5 ANSWER 30 OF 53 DISSABS COPYRIGHT (C) 2007 ProQuest Information and Learning Company; All Rights Reserved on STN
ACCESSION NUMBER: 2003:29641 DISSABS Order Number: AAIC809995 (not available for sale by UMI)
TITLE: Cellular interactions with extracellular matrix during development and in muscle disease
AUTHOR: Tiger, Carl-Fredrik [Ph.D.]
CORPORATE SOURCE: Uppsala Universitet (Sweden) (0903)
SOURCE: Dissertation Abstracts International, (2002) Vol. 63, No. 4C, p. 723. Order No.: AAIC809995 (not available for sale by UMI). Uppsala University Library, Box 510, SE-751 20 Uppsala, Sweden. 39 pages.
ISBN: 91-554-5328-7.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English

AB The formation and maintenance of tissues in multicellular animals are crucially dependent on cellular interactions with the extracellular matrix (ECM). Two different studies on such interactions are presented herein.

Studies on expression of laminins in normal and dystrophic skeletal muscle, clarified a much debated issue regarding discrepancies seen for laminin $\alpha 1$ -chain expression between human and mouse tissues. Lack of laminin $\alpha 1$ -chain expression was verified in both mouse and human skeletal muscle. Furthermore, the earlier discrepancies seen for laminin $\alpha 1$ -chain expression was explained by showing that an antibody-reagent, commonly used in human studies, recognised the laminin $\alpha 5$ -chain rather than the laminin $\alpha 1$ -chain.

The integrin .alpha.11-chain (forming .alpha.11 β 1 integrin) is the latest addition to the integrin receptor family, and belongs to the I domain-containing group of integrin α -chains. Previous studies had shown that .alpha.11 β 1 is a collagen receptor. In the present study, the in vitro and in vivo functions of the .alpha.11-chain were further characterised. Distribution studies on embryonic human and mouse tissues showed that the .alpha.11-chain was expressed on mesenchymal cells in the developing tendon, perichondrium, intervertebral disc, and cornea. The interactions of .alpha.11 β 1 integrin with collagen type I and IV were studied in vitro. The .alpha.11 β 1 bound to these collagens in a manner similar to integrin $\alpha 2\beta 1$ (with collagen type I being the preferred ligand for .alpha.11 β 1). Furthermore, .alpha.11 β 1 was shown to mediate migration on collagen type I coated surfaces, and to mediate contraction of collagen type I gels. The in vivo functions of the .alpha.11-chain were investigated by the generation of integrin .alpha.11-chain null-mice, using gene targeted disruption of the itgall in embryonic stem cells. Two independent lines of mice lacking .alpha.11 protein were generated. Phenotypic analysis of these mice indicated a role for .alpha.11 β 1 in the formation of the musculoskeletal system.

AB . . . that an antibody-reagent, commonly used in human studies, recognised the laminin $\alpha 5$ -chain rather than the laminin $\alpha 1$ -chain.

L5 ANSWER 29 OF 53 \CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:859070 CAPLUS

DOCUMENT NUMBER: 142:20235

TITLE: Structure and function of $\alpha 11\beta 1$ integrin

AUTHOR(S): Gullberg, Donald; Popova, Svetlana N.; Tiger, Carl-Fredrik

CORPORATE SOURCE: Department of Medical Biochemistry and Microbiology, Uppsala University, Uppsala, Swed.

SOURCE: I Domains in Integrins (2003), 67-81. Editor(s): Gullberg, Donald. Landes Bioscience: Georgetown, Tex. CODEN: 69FYF3; ISBN: 0-306-47836-6

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review. The $\alpha 11$ integrin chain constitutes the latest addition to the integrin family. $\alpha 11\beta 1$ Was originally identified on cultured human muscle cells, but recent studies have shown that it is not expressed on muscle cells in vivo. It remains to be determined if satellite cells in regenerating muscle express $\alpha 11$. Distribution data indicate that the .alpha.11 chain in vivo is expressed on a subset of mesenchymal cells in the developing human embryo. Expression is high in the developing musculoskeletal system in areas of cartilage, bone and in tendon formation. High .alpha.11 expression is also seen in mesenchymal tissues characterized by elaborately organized collagen matrixes such as the intervertebral disk and the cornea. In agreement with the distribution data, ligand binding studies suggest that $\alpha 11$ prefers collagen I over collagen IV. We will review the current knowledge about $\alpha 11\beta 1$ and discuss the possible in vivo functions of $\alpha 11\beta 1$ and also address the issue of functional redundancy among collagen-binding integrins.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A review. The $\alpha 11$ integrin chain constitutes the latest addition to the integrin family. $\alpha 11\beta 1$ Was originally identified on cultured human muscle cells, but recent studies have shown that it is not expressed on muscle cells in vivo. It remains to be determined if satellite cells in regenerating muscle express $\alpha 11$. Distribution data indicate that the .alpha.11 chain in vivo is expressed on a subset of mesenchymal cells in the developing human embryo. Expression is high in the developing musculoskeletal system in areas of cartilage, bone and in tendon formation. High .alpha.11 expression is also seen in mesenchymal tissues characterized by elaborately organized collagen matrixes such as the intervertebral disk and the cornea. In agreement with the distribution data, ligand binding studies suggest that $\alpha 11$ prefers collagen I over collagen IV. We will review the current knowledge about $\alpha 11\beta 1$ and discuss the possible in vivo functions of $\alpha 11\beta 1$ and also address the issue of functional redundancy among collagen-binding integrins.

ACCESSION NUMBER: 2004:82805 LIFESCI

TITLE: The mesenchymal alpha 11
beta 1 integrin attenuates PDGF-BB-stimulated chemotaxis of
embryonic fibroblasts on collagensAUTHOR: Popova, S.N.; Rodriguez-Sanchez, B.; Liden, A.; Betsholtz,
C.; Van den Bos, T.; Gullberg, D.CORPORATE SOURCE: Department of Medical Biochemistry and Microbiology,
Biomedical Center, Uppsala, Sweden; E-mail:
donald.gullberg@biomed.uib.noSOURCE: Developmental Biology [Dev. Biol.], (20040600) vol. 270,
no. 2, pp. 427-442.
ISSN: 0012-1606.

DOCUMENT TYPE: Journal

FILE SEGMENT: N

LANGUAGE: English

SUMMARY LANGUAGE: English

AB alpha 11 beta 1 constitutes the most recent addition to the integrin family and has been shown to display a binding preference for interstitial collagens found in mesenchymal tissues. We have previously observed that when alpha 11 beta 1 integrin is expressed in cells lacking endogenous collagen receptors, it can mediate PDGF-BB-dependent chemotaxis on collagen I in vitro. To determine in which cells PDGF and alpha 11 beta 1 might cooperate in regulating cell migration in vivo, we studied in detail the expression and distribution of alpha 11 integrin chain in mouse embryos and tested the ability of PDGF isoforms to stimulate the alpha 11 beta 1-mediated cell migration of embryonic fibroblasts. Full-length mouse alpha 11 cDNA was sequenced and antibodies were raised to deduced alpha 11 integrin amino acid sequence. In the embryonic mouse head, alpha 11 protein and RNA were localized to ectomesenchymally derived cells. In the periodontal ligament, alpha 11 beta 1 was expressed as the only detectable collagen-binding integrin, and alpha 11 beta 1 is thus a major receptor for cell migration and matrix organization in this cell population. In the remainder of the embryo, the alpha 11 chain was expressed in a subset of mesenchymal cells including tendon/ligament fibroblasts, perichondrial cells, and intestinal villi fibroblasts. Most of the alpha 11-expressing cells also expressed the alpha 2 integrin chain, but no detectable overlap was found with the alpha 1 integrin chain. In cells expressing multiple collagen receptors, these might function to promote a more stable cell adhesion and render the cells more resistant to chemotactic stimuli. Wild-type embryonic fibroblasts activated mainly the PDGF beta receptor in response to PDGF-BB and migrated on collagens I II III IV, V, and XI in response to PDGF-BB in vitro, whereas mutant fibroblasts that lacked alpha 11 beta 1 in their collagen receptor repertoire showed a stronger chemotactic response on collagens when stimulated with PDGF-BB. In the cellular context of embryonic fibroblasts, alpha 11 beta 1 is thus anti-migratory. We speculate that the PDGF BB-dependent cell migration of mesenchymal cells is tightly regulated by the collagen receptor repertoire, and disturbances of this repertoire might lead to unregulated cell migration that could affect normal embryonic development and tissue structure.

TI The mesenchymal alpha 11 beta 1 integrin attenuates PDGF-BB-stimulated chemotaxis of embryonic fibroblasts on collagens

AB alpha 11 beta 1 constitutes the most recent addition to the integrin family and has been shown to display a binding preference for interstitial collagens found in mesenchymal tissues. We have previously observed that when alpha 11 beta 1 integrin is expressed in cells lacking endogenous collagen receptors, it can mediate PDGF-BB-dependent chemotaxis on collagen I in vitro. To determine

in which cells PDGF and alpha 11 beta 1 might cooperate in regulating cell migration in vivo, we studied in detail the expression and distribution of alpha 11 integrin chain in mouse embryos and tested the ability of PDGF isoforms to stimulate the alpha 11 beta 1-mediated cell migration of embryonic fibroblasts. Full-length mouse alpha 11 cDNA was sequenced and antibodies were raised to deduced alpha 11 integrin amino acid sequence. In the embryonic mouse head, alpha 11 protein and RNA were localized to ectomesenchymally derived cells. In the periodontal ligament, alpha 11 beta 1 was expressed as the only detectable collagen-binding integrin, and alpha 11 beta 1 is thus a major receptor for cell migration and matrix organization in this cell population. In the remainder of the embryo, the alpha 11 chain was expressed in a subset of mesenchymal cells including tendon/ligament fibroblasts, perichondrial cells, and intestinal villi fibroblasts. Most of the alpha 11-expressing cells also expressed the alpha 2 integrin chain, but no detectable overlap was found with the alpha 1 integrin chain. . . . on collagens I II III IV, V, and XI in response to PDGF-BB in vitro, whereas mutant fibroblasts that lacked alpha 11 beta 1 in their collagen receptor repertoire showed a stronger chemotactic response on collagens when stimulated with PDGF-BB. In the cellular context of embryonic fibroblasts, alpha 11 beta 1 is thus anti-migratory. We speculate that the PDGF BB-dependent cell migration of mesenchymal cells is tightly regulated by the collagen receptor repertoire, and disturbances of this repertoire might lead to unregulated cell migration. . . .

ACCESSION NUMBER: 2006:314910 BIOSIS
DOCUMENT NUMBER: PREV200600312498
TITLE: Tandem Sp1/Sp3 sites together with an Ets-1 site cooperate
to mediate alpha 11 integrin chain
expression in mesenchymal cells.
AUTHOR(S): Lu, Ning; Heuchel, Rainer; Barczyk, Malgorzata; Zhang,
Wan-Ming; Gullberg, Donald [Reprint Author]
CORPORATE SOURCE: Univ Bergen, Dept Biomed, Div Physiol, Jonas Lies Vei 91,
N-5009 Bergen, Norway
donald.gullberg@biomed.uib.no
SOURCE: Matrix Biology, (MAR 2006) Vol. 25, No. 2, pp. 118-129.
ISSN: 0945-053X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Jun 2006
Last Updated on STN: 14 Jun 2006

- AB all 1 integrin is a collagen receptor, which is expressed in a highly regulated manner in a specific subset of ectomesenchymally and mesodermally derived cells. We previously established that a 3 kb region upstream of the transcription start site of the ITGA11 gene efficiently induced alpha 11 transcription in a cell-type specific manner. Using the human fibrosarcoma cell line HT 1080 and human skin fibroblasts, we now report that the majority of the activity in the proximal promoter resides in a region spanning nt +25 to nt -176. Mutation and deletion analyses using luciferase reporter assays showed that tandem low affinity Sp1/Sp3 binding sites, together with an Ets-1-like binding site, were needed for the proximal promoter activity in mesenchymal cells. EMSAs and supershift assays showed that Sp1 and Sp3 both bind to the Sp1/Sp3 binding sites, whereas occupation of the Ets-1 binding site appears to be Sp3-dependent. Chromatin immunoprecipitation assays verified that Sp1, Sp3 and Ets-1 can bind the promoter in vivo. In heterologous Drosophila SL2 cells, Sp1, Sp3 and Ets-1 all transactivated the alpha 11 promoter, with Sp1 being the most efficient activator. The lack of any synergistic effect of Sp1/Sp3 and Ets-1 in SL2 cells indicates that an Ets family member other than Ets-1 might be involved in regulating alpha 11 transcription in mesenchymal cells. The central role of Sp1 in regulating alpha 11 RNA transcription was further verified by the ability of the Sp1 inhibitor mithramycin A to efficiently attenuate alpha 11 RNA and protein levels in primary fibroblasts. The proximal promoter itself was able to confer cell-type specific transcription on HT1080 cells and embryonic fibroblasts but not on U2OS and JAR cells. We speculate that the "mesenchymal signature" of alpha 11 integrin gene expression is controlled by the activity of Sp1/Sp3, fibroblast-specific combinations of Ets family members and yet unidentified enhancer-binding transcription factors. (c) 2005 Elsevier B.V./International Society of Matrix Biology. All rights reserved.
- TI Tandem Sp1/Sp3 sites together with an Ets-1 site cooperate to mediate alpha 11 integrin chain expression in mesenchymal cells.
- AB. . . Sp1/Sp3 and Ets-1 in SL2 cells indicates that an Ets family member other than Ets-1 might be involved in regulating alpha 11 transcription in mesenchymal cells. The central role of Sp1 in regulating alpha 11 RNA transcription was further verified by the ability of the . . . cell-type specific transcription on HT1080 cells and embryonic fibroblasts but not on U2OS and JAR cells. We speculate that the "mesenchymal signature" of alpha 11 integrin gene expression is controlled by the activity of Sp1/Sp3, fibroblast-specific combinations of Ets family members and yet unidentified enhancer-binding. . .

L5 ANSWER 5 OF 53 USPATFULL on STN

ACCESSION NUMBER: 2006:95175 USPATFULL
TITLE: Integrin heterodimer and a subunit thereof
INVENTOR(S): Lundgren-Åkerlund, Evy, Bjarred, SWEDEN
PATENT ASSIGNEE(S): Cartela AB, Bjarred, SWEDEN (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 7029858	B1	20060418
	WO 9951639		19991014
APPLICATION INFO.:	US 1999-647544		19990331 (9)
	WO 1999-SE544		19990331
			20000426 PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	SE 1998-1164	19980402
	SE 1999-319	19990128
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Chan, Christina	
ASSISTANT EXAMINER:	Haddad, Maher M.	
LEGAL REPRESENTATIVE:	Buchanan Ingersoll PC	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	23 Drawing Figure(s); 23 Drawing Page(s)	
LINE COUNT:	3572	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A recombinant or isolated integrin heterodimer comprising a novel subunit $\alpha 10$ in association with a subunit β is described. The $\alpha 10$ integrin may be purified from bovine chondrocytes on a collagen-type-II affinity column. The integrin or the subunit $\alpha 10$ can be used as marker or target of all types of cells, e.g. of chondrocytes, osteoblasts and fibroblasts. The integrin or subunit $\alpha 10$ thereof can be used as marker or target in different physiological or therapeutic methods. They can also be used as active ingredients in pharmaceutical compositions and vaccines.

DETD A polyclonal peptide antibody raised against the cytoplasmic domain of $\alpha 10$ precipitated two protein bands with M.sub.r of approximately 160 kD ($\alpha 10$) and 125 kD ($\beta 1$) under reducing conditions. Immunohistochemistry using the $\alpha 10$ -antibody showed staining of the chondrocytes in tissue sections of human articular cartilage. The antibody staining was clearly specific since preincubation of the antibody with the $\alpha 10$ -peptide completely abolished the staining. Immunohistochemical staining of mouse limb sections from embryonic tissue demonstrated that $\alpha 10$ is upregulated during condensation of the mesenchyme. This indicate that the integrin subunit $\alpha 10$ is important during the formation of cartilage. In 3 day old mice $\alpha 10$ was found to be the dominating collagen binding integrin subunit which point to that $\alpha 10$ has a key function in maintaining normal cartilage functions.

DETD FIG. 11 show that $\alpha 10$ integrin subunit is unregulated in the limb when the mesenchymal cells undergo condensation to form cartilage (a). Especially the edge of the newly formed cartilage has high expression of $\alpha 10$. The formation of cartilage is verified by the high expression of the cartilage specific collagen type II (b). The control antibody against $\alpha 1$ integrin subunit showed only weak expression on the cartilage (c). In other experiments expression of $\alpha 10$ was found in all cartilage containing tissues in the 3 day old mouse including limbs, ribs and vertebrae. The upregulation of $\alpha 10$

.10 during formation of cartilage suggest that this integrin subunit is important both in the development of cartilage and bone and.

. . .

Two relatively newly discovered integrins, $\alpha 10$ ^{38, 39} and $\alpha 11$, ^{40, 41} have been shown to be collagen receptors that are expressed in cartilage. $\alpha 10$ has a cellular distribution that differs from $\alpha 1$ and $\alpha 2$ and is the dominant integrin during embryonic development. ³⁹ $\alpha 10$ preferentially binds basement membrane collagens, as $\alpha 1$, whereas $\alpha 11$ resembles $\alpha 2$ showing specificity for fibril forming collagens. ⁴²